## DETAILED ACTION

The amendment filed January 21, 2011 (hereinafter referred to as "the response") has been entered. Claims 59-65, 67, 78, 86, 89, 90, 104, 105, 106, and 108 have been amended. Claims 103, 107, and 109 have been cancelled and Claims 110 and 111 have been newly added.

Accordingly, Claims 59-65, 67, 68, 71-78, 80-86, 88-90, 92-102, 104-106, 108, 110 and 111 are pending in the instant application.

The elected invention is drawn to a dental pulp multipotent stem cell.

Claims 67, 68, 71-78, 80-86, 88-90, 92-102, and 108 remain withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on December 9, 2009.

Accordingly, Claims 59-65, 104-106, 110, and 111 are examined herein.

### Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on January 21, 2011 has been entered.

The objection to Claim 103 under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim, is **withdrawn** in view of the cancellation of the claim.

The Declaration of Dr. Akiyama has been fully considered and is accepted as showing that a biological deposit was made and that the material deposited therein was the biological material identified in the patent application as originally filed.

## Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

### New Matter

Claims 59-65, 104-106 stand rejected and Claims 110 and 111 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The amended claims and newly added claims include new matter.

MPEP 2163.03(I) provides that an amendment to the claims or the addition of a new claim must be supported by the description of the invention in the application as filed. In re Wright, 866 F.2d 422, 9 USPQ2d 1649 (Fed. Cir. 1989). Applicants should specifically point out the support for any amendments made to the claims. MPEP 2163 states that new or amended claims which introduce elements or limitations which are not supported by the as-filed disclosure violate the written description requirement. See, e.g., In re Lukach, 442 F.2d 967, 169 USPQ 795 (CCPA 1971) and In re Smith, 458 F.2d 1389, 1395, 173 USPQ 679, 683 (CCPA 1972). MPEP 714.02 notes that Applicant should also specifically point out the support for any amendments made to the disclosure. See also MPEP 2163.06(I), which

notes that Applicants should specifically point out the support for any amendments made to the disclosure.

In the amendment filed April 1, 2010, the claims were amended to add the limitation "wherein the isolated human postnatal dental pulp multipotent stem cell can proliferate to over 140 population doublings." In the amendment filed January 21, 2011, Claim 59 was further amended to add the limitation "wherein stem cells in the population induce the formation of bone when transplanted in vivo." Accordingly, Claim 59 is directed to a CD146-positive cell that can proliferate to over 140 population doublings and also possesses the ability to induce the formation of bone when transplanted in vivo. However, the specification does not describe a CD146-positive cell that can proliferate to over 140 population doublings. On the contrary, the specification only describes a mixed population of cells (SHED) that can proliferate to over 140 population doublings. Likewise, the specification does not describe a CD146-positive cell that has the ability to induce the formation of bone when transplanted in vivo. On the contrary, the specification only describes clonal cells that have the ability to induce the formation of bone when transplanted in vivo, but these clones are not defined by any particular cell markers (page 28, lines 5-11).

In the reply filed April 1, 2010, as support for the amendment reciting 140 population doublings, Applicants pointed to the specification at page 7, lines 10-15 and Figure 5. However, the cited section clearly describes a mixed population of cells, designated as "SHED." The assessment of proliferation in terms of population doublings was carried out using this mixed population of cells (SHED). Notably, the specification does not provide an assessment of the proliferation of any particular cell type present within the mixed population. Thus, the rate of proliferation of the multipotent stem cell that is identified as residing within this mixed population of cells is unknown. Accordingly, the specification fails to describe a multipotent stem cell that can proliferate to over 140 population doublings. Instead, the specificationd describes a mixed population of cells (SHED) which can proliferate to over 140 population doublings.

The proliferative capacity of any cell type within the mixed population is unknown. Thus, there is no evidence that a CD146-positive cell can proliferate to over 140 population doublings. Accordingly, there is no evidence that Applicants were in possession of a CD146-positive cell that can proliferate to over 140 population doublings.

Newly added Claims 110 and 111 depend from Claim 59 and therefore incorporate all the limitations of independent Claim 59. Although Claim 110 recites an ATCC deposit number, the claim is not directed to the deposited cells per se, but instead is only directed to cells that have the characteristics of the deposited cells in addition to the properties recited in the limitations of Claim 59. As discussed above, the specification does not describe a population of cells having the properties recited in Claim 59. Claim 111 is directed to a clonal cell isolated from the isolated population of human postnatal deciduous dental pulp multipotent stem cells of Claim 59. However, the specification does not describe a clonal cell that can proliferate to over 140 population doublings, nor does it describe a clonal cell that expresses CD146. Thus, the specification clearly fails to describe a CD146-positive clonal cell that can proliferate to over 140 population doublings.

As amended, Claim 59 is directed to a CD146-positive multipotent stem cell that can proliferate to over 140 population doublings and can differentiate into a neural cell, an adipocyte, or an odontoblast, and further possesses the ability to induce the formation of bone when transplanted in vivo. However, there is no description of a CD146-positive cell that can proliferate to over 140 population doublings. While the specification does disclose that SHED were able to proliferate to over 140 population doublings (page 7, line 14), the specification makes it clear that SHED is a mixed population of cells (pages 27-28). See for example, the specification at page 8, lines 10-17, which discloses that only 25% of SHED clones were capable of generating dentin in vivo. At page 7, lines 17-21, the specification discloses that SHED expressed STRO-1 and CD146 and that FACS analysis of ex vivo expanded SHED showed that SHED contained approximately 9% STRO-1-positive cells. The specification is silent as to the percentage of

SHED expressing CD146. However, there is no disclosure of CD146-positive cells that have the potential to undergo 140 population doublings. Only the mixed population of SHED is described as having the ability to proliferate to over 140 population doublings (page 7, lines 14-15 and Figure 5H).

Likewise, with regard to Claim 61, the specification does not describe a STRO-1-positive cell that can proliferate to over 140 population doublings. Nor does the specification describe an ALP-positive cell that can proliferate to over 140 population doublings. Nor does the specification describe a matrix extracellular phosphoglycoprotein-positive cell that can proliferate to over 140 population doublings. Nor does the specification describe an bFGF-positive cell that can proliferate to over 140 population doublings. Nor does the specification describe an endostatin-positive cell that can proliferate to over 140 population doublings. Nor does the specification describe a cell that expresses a combination of these proteins and that can also proliferate to over 140 population doublings.

Likewise, with regard to Claim 62, the specification does not describe a CBFA1-positive cell that can proliferate to over 140 population doublings. Nor does the specification describe an MEPE-positive cell that can proliferate to over 140 population doublings. Nor does the specification describe an BSP-positive cell that can proliferate to over 140 population doublings. Nor does the specification describe an DSPP-positive cell that can proliferate to over 140 population doublings. Nor does the specification describe a cell that expresses a combination of these proteins and that can also proliferate to over 140 population doublings.

Likewise, with regard to Claim 63, the specification does not describe a osterix-positive cell that can proliferate to over 140 population doublings. Nor does the specification describe an osteocalcin-positive cell that can proliferate to over 140 population doublings. Nor does the specification describe a cell that expresses a combination of these proteins and that can also proliferate to over 140 population doublings.

Likewise, with regard to Claim 64, the specification does not describe a nestin-positive cell that can proliferate to over 140 population doublings. Nor does the specification describe an βIII tubulin-positive cell that can proliferate to over 140 population doublings. Nor does the specification describe a glutamic acid decarboxylase-positive cell that can proliferate to over 140 population doublings. Nor does the specification describe a neuronal nuclei-positive cell that can proliferate to over 140 population doublings. Nor does the specification describe a glial fibrillary acidic protein-positive cell that can proliferate to over 140 population doublings. Nor does the specification describe a neurofilament M-positive cell that can proliferate to over 140 population doublings. Nor does the specification describe a 2'3'-cyclic nucleotide-3'-phosphodiesterase-positive cell that can proliferate to over 140 population doublings. Nor does the specification describe a cell that expresses a combination of these proteins and that can also proliferate to over 140 population doublings.

Given the many dependent claims to isolated human postnatal deciduous dental pulp stem cells, Claim 59 appears to cover a wide variety of stem cells expressing distinct sets of markers. Accordingly, Claim 59 is further rejected insofar as it encompasses the various cell types recited in Claims 61-65 because the specification fails to describe all the cell types encompassed by Claim 59. The dependent claims appear to be directed to various subsets of stem cells that fall within the broad independent claim (i.e., Claim 59), but there is no description of distinct multipotent stem cells that are CD146-positive and that can proliferate to over 140 population doublings.

Since the as-filed specification does not describe the subject matter of Claim 59 and the various cell types recited in the dependent claims, claims directed to subject matter not disclosed in the originally filed specification cannot be introduced after the application filing date. Such a claim raises an issue of new matter. Given the new limitations added by amendment, the specification would have to provide support for the multipotent stem cell of Claim 59, in its broadest sense, and multiple distinct cell types as set forth in the dependent claims. However, the specification does not provide broad support, nor does it

provide narrower support for cells expressing the various proteins recited in the claims and also having the ability to proliferate to over 140 population doublings. Thus, the as-filed specification does not provide adequate support for the amended claims and newly added claims.

Thus, the amended claims and newly added claims include new matter.

At page 10 of the response, Applicants assert that clonal cell populations of SHED cells are described in the specification at page 27, line 29 and that all of these clonal populations of cells induce bone formation upon transplantation. Applicants further assert, citing Figures 9 and 10, pages 16-17, and pages 27-28, that these cells also differentiate into cells expressing neurofilament and can form adipose tissue. However, these arguments do not address the new matter rejection. There is no evidence demonstrating support for a CD146-positive cell that has the ability to undergo 140 population doublings.

At pages 10-11 of the response, Applicants assert that the claimed cell populations and clonal cell are distinct from the cells disclosed in the prior art of record. No art rejections are made against the present claims.

**Conclusion**

No claims are allowable.

All claims are drawn to the same invention claimed in the application prior to the entry of the submission under 37 CFR 1.114 and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the application prior to entry under 37 CFR 1.114. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action after the filing of a request for continued examination and the submission under 37 CFR 1.114. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing

date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne-Marie Falk whose telephone number is (571) 272-0728. The examiner can normally be reached Monday through Friday from 9:00 AM to 5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras, can be reached on (571) 272-4517. The central official fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

/Anne-Marie Falk/
Primary Examiner, Art Unit 1632